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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/065,856	11/26/2002	Ann E. Loraine	3291.3A	3379

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AFFYMETRIX, INC
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EXAMINER

MILLER, MARINA I

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 02/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/065,856	LORAIN ET AL.	
	Examiner	Art Unit	
	Marina Miller	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 January 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-45 is/are pending in the application.
- 4a) Of the above claim(s) 10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 and 11-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 26 November 2002 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>2/09/2004</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION***Election/Restrictions***

Applicant's election with traverse of Species A (nucleic acids), Species B (model fitting), Species C (mRNA), and Species D (enabling) in the reply filed on 01/07/2005 is acknowledged. The traversal is on the ground(s) that elected species of mRNA recited in claims 16, 33, and 44 is patentably distinct from species recited in claims 17, 34, and 45. This is not found persuasive. It is recognized that two sets of claims (1) 16, 33, and 44 and (2) 17, 34, and 45 are directed to an annotated datum to be selected or displayed. Both sets of claims provide for different groups/species of the annotated datum. Claims 16, 33, and 44 recite fewer species than claims 17, 34, and 45, which are a subset of those recited in claims 17, 34, and 45. Both recite mRNA. Thus, examiner treats the election of species of mRNA as being elected for annotated datum of claims 16, 17, 33, 34, 44, and 45.

Claim 10 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claims.

The requirement is still deemed proper and is therefore made FINAL.

Priority

Applicant's claim for priority under 35 U.S.C. 119(e), 120, and 122 is acknowledged. However, the applications for which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 1-45 of the instant application.

Applicant claims priority to a series of provisional, non-provisional, and PCT applications. Examiner thoroughly reviewed all priority applications. None of the priority

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applications provide support for claims 1-45 of the instant application drawn to a method and a system for providing information about biological molecules. The priority applications do not disclose the method of claim 1 comprising steps: receiving a probe identifiers, determining alternative splice variants, correlating splice variants with annotated data, and providing a graphical representation of splice variant and annotated datum. The applications also do not provide support for the method of claim 3 comprising steps: determining alternative splice variants, correlating splice variants with annotated data, and enabling for displaying splice variant and annotated datum. These applications also do not provide support for a system of claim 28 and a genomic portal system of claim 43.

If applicant desires benefit of these priority applications, applicant is invited to point to specific support by page and line number for each limitation of the instant claims in each priority applications. As support for the elected claims is not found in the priority applications, priority for the elected claims is granted only to the filing date of the instant application of 11/26/2002.

Oath/Declaration

Oath/Declaration was filed 11/27/2003. Due to a scanning problem, the document shows up blank. The examiner regrets the inconvenience to applicant. Applicant is kindly requested to supply another copy of the executed declaration.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, such as in paragraphs [0074] and [0076]. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Drawings

The drawings are objected to because they do not comply with 37 CFR 1.84 and 37 CFR 1.121, as set forth in the letter mailed 12/18/02. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 101

Lack of Utility

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

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Claims 1, 3-9, and 11-45 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The specification discloses that utility for the claimed invention is a use of microarray data to study genetic characteristics and detect diseases. In particular, to detect what genes are expressed in particular tumors, organs, tissues, or species and how different factors influence gene expression (see p. 3 of the specification). However the disclosed utility is not applicable to the instant claims. For example, the result of the claimed methods is displaying splice variants determined on the basis of a probe array for unknown nucleic acids and correlated to the splice variants' unknown annotation datum. In order for the result of the method to be used for diagnostic purposes, one skilled in the art must be aware of a correlation between the information retrieved and a disease, disorder, or condition to be diagnosed. No such correlation is recited in the instant claim; further research would be required to determine such a correlation. Applicant is reminded that a "use" to perform further research is not a utility under 35 U.S.C. 101. In the absence of recitation of specific tissues, cells, etc., known to be correlated to a disease, disorder, condition, etc., for diagnosis; or recitation of specific genetic information with a similar correlation (e.g., haplotype frequency, SNP, splice variants, etc. known to be associated with a disease or propensity for disorder/disease), the claims do not provide an "immediate benefit" to the public, and lack utility.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3, 4, 6-9, 11, 12, 16-22, 24-28, 31, 33-37, 40-42 are rejected under 35

U.S.C. 102(b) as being anticipated by Hu, *Genome Research*, 11(7):1237-45 (July 2001).

Hu discloses a method similar to the method recited in instant claim 1. Steps of receiving a probe set identifier (*i.e.*, hybridization data for a custom array of 1600 rat genes) that identifies a probe array (p. 1237, right col.), determining alternative splice variants (p. 1237, 1238 and fig. 2), correlating splice variants to annotated data (fig. 3 and 4, table 3), and providing to the user a graphical representation of splice variants and annotated datum (p. 1239, fig. 3 and 4. Thus, Hu anticipates the instant claim 1.

Hu discloses steps of the instant method 3: determining splice variants based on probe set identifier that identifies probe sets (p. 1238), correlating splice variants with annotated data (fig. 3 and 4, table 3), and enabling for display (fig. 3 and 4), thus anticipating instant claim 3.

Hu discloses a system comprising a splice variant evaluator (*i.e.*, Affymetrix DNA chip, a scanner, and a computer program), p. 1243-44; data storage and annotation data correlator (fig. 3); and a manager to enable for displaying splice variants and annotated data (p. 1239, left col., Spotfire Pro 4.0 software tool, and fig. 3), thus anticipating claim 28.

Hu discloses receiving hybridization data for a custom array of 1600 rat genes (p. 1237), thus anticipating claim 4. Hu discloses a synthesized and spotted array wherein probes disposed

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on a glass chip (p. 1237, left col. and p. 1243-44), thus anticipating claims 6 and 7. Hu discloses a probe array for detection of nucleic acids (p. 1237 and 1244), thus anticipating claims 8 and 31. Hu discloses determining splice variants by algorithms comprising normalization (p. 1244, Processing Data and SPLICE Algorithm), thus anticipating claim 9. Hu discloses correlation of a splice variant with a gene and correlation the gene with an annotated datum (*see* tables 2-3 and p. 1239-40), thus anticipating claim 11. Hu discloses correlation of splice variants of their common gene and correlation of splice variant to annotated datum (fig. 3), thus anticipating claim 12. Hu discloses a display set up for displaying annotation datum such as mRNA (fig. 3B), thus anticipating claims 16 and 33. Hu discloses annotation datum as being mRNA (fig. 3), thus anticipating claims 17 and 34.

Hu discloses aligning of splice variants (fig. 3B), thus anticipating claims 18 and 35. Hu discloses aligning of splice variants compared to a sequence of the same gene (fig. 3B and p. 1239), thus anticipating claims 19 and 36. Hu discloses graphical associating splice variants (fig. 3-4), thus anticipating claims 20 and 37. Hu discloses separate displaying splice variants in a plurality of panels (fig. 3A and 4), thus anticipating claim 21. Hu discloses receiving hybridization data for a custom DNA array of 1600 rat genes and providing splice variants correlated with annotated data (p. 1237 and 1243-44), thus anticipating claim 22. Hu discloses probes for detecting mRNA expression (p. 1237 and fig. 1), thus anticipating claims 24 and 40. Hu discloses adjacent probes (p. 1244, Neighborhood Algorithm), thus anticipating claims 25 and 41. Hu discloses receiving hybridization intensities from biological array and determining splice variants on the basis of hybridization intensities (p. 1237 and 1238), thus anticipating claims 26, 27, and 42.

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Claim 43-45 are rejected under 35 U.S.C. 102(a) and (e) as being anticipated by Wang, US 2002/0029113.

Wang teaches a genomic web portal recited in instant claim 43. Wang discloses a system for predicting alternative splice transcripts using DNA chip expression data. Wang's web portal is generally disclosed in fig. 1. The detailed description of the portal is disclosed in [0025-0035 and 0037-0038]. The portal comprises an input manager to receive user's selection of probe identifier and hybridization intensities obtained from a probe array, a splice variants evaluator, a data storage and annotation data correlator, a user-server manager to enable for display, and an output manager constructed to send to the user over the Internet splice variants and annotated datum, [0025-0035 and 0037-0038]. Wang discloses annotation datum as being mRNA [0066], thus anticipating claims 44 and 45.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hu, *Genome Research*, 11(7):1237-45 (July 2001), as applied to claim 1 above, in view of Phillips, U.S. Patent 6,171,793.

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Hu teaches the method of claim 1, as set forth above.

Hu does not teach a probe array constructed to diagnose disease.

Phillips discloses using a probe array for detecting disease, col. 2, line 65-67-col.3, line 1-11.

It would have been obvious to one skilled in the art at the time of the invention to modify the method of Hu to use a probe array for detecting diseases, such as taught by Phillips, where the motivation would have been to achieve an efficient and simultaneous analysis of multiple genes associated with defects, as taught by Phillips, col. 3, line 11-19.

Claims 5 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hu, *Genome Research*, 11(7):1237-45 (July 2001), as applied to claim 3-4, 6-9, 11-12, 16-22, and 24-27 above, in view of Wang, US 2002/0029113.

Hu teaches steps of the method of instant claim 3 wherein probe set identifier are received from a user, and splice variants information is provided, as set forth above.

Hu does not disclose that the receiving a probe set identifier or providing to the user splice variants are accomplished over the Internet, intranet or LAN.

Wang discloses a system for determining splice variants wherein a user terminal is connected to a server via a network or the Internet, [0025-0026].

It would have been obvious to one skilled in the art at the time of the invention to modify the method of Hu to utilize network communication between a user and a server, such as taught by Wang, where the motivation would have been to achieve an efficient and simultaneous

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analysis of multiple genes using public/private annotated databases and new algorithms to learn splicing of tens thousands of genes, as taught by Wang, [0011-0012].

Claims 29, 30, 38, and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hu, *Genome Research*, 11(7):1237-45 (July 2001), as applied to claim 28, 31, 33-37, and 40-42 above, in view of Wang, US 2002/0029113.

Hu teaches the system of instant claim 28, as set forth above.

Hu does not disclose an input manager constructed to receive from a user a probe set identifier, as recited in claim 29 and receiving over the Internet, as recited in claim 30. Hu does not disclose an input and output manager utilizing a network or the Internet, as recited in claims 38-39.

Wang discloses a system for determining splice variants wherein a user terminal is connected to a server via a network or the Internet, [0025-0026]. The user's system may upload information to the server over the Internet or may download information from a server or a database [0026]. Wang also discloses the expression subsystem (input or output data) using a network interface and a user interface including a display. The network interface provides an access to networks, *e.g.*, Internet, [0029].

It would have been obvious to one skilled in the art at the time of the invention to modify the system of Hu to utilize network communication between a user and a server, such as taught by Wang, where the motivation would have been to achieve an efficient and simultaneous analysis of multiple genes using public/private annotated databases and new algorithms to learn splicing of tens thousands of genes, as taught by Wang, [0011-0012].

Claims 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hu, *Genome Research*, 11(7):1237-45 (July 2001), as applied to claim 3-4, 6-9, 11-12, 16-22, 24-27 above, in view of Helt, *Genomic Research*, 8(3):291-305 (1998).

Hu teaches steps of the method of instant claim 3, as set forth above.

Hu does not disclose semantic zooming, as recited in instant claim 13; annotation datum displayed on a sequence axis, as recited in claim 14; and displaying capable of collapsing or moving, as recited in claim 15.

Helt discloses semantic zooming (p. 299), annotation datum displayed on a sequence axis (fig. 2), and displaying capable of collapsing or moving (fig. 3).

It would have been obvious to one skilled in the art at the time of the invention to modify the method of Hu to utilize zooming system, such as taught by Helt, where the motivation would have been to obtain visualization tools for bioinformatics and provide an efficient access to sequence databases, as taught by Helt, p. 291.

Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hu, *Genome Research*, 11(7):1237-45 (July 2001), as applied to claim 28, 31, 33-34, 40-42 above, in view of Helt, *Genomic Research*, 8(3):291-305 (1998).

Hu teaches steps of the system of instant claim 3, as set forth above.

Hu does not disclose semantic zooming, as recited in instant claim 32.

Helt discloses semantic zooming (p. 299).

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It would have been obvious to one skilled in the art at the time of the invention to modify the method of Hu to utilize zooming system, such as taught by Helt, where the motivation would have been to obtain visualization tools for bioinformatics and provide an efficient access to sequence databases, as taught by Helt, p. 291.

Conclusion

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Schena, PNAS, 93:10614-19 (1996) (disclosing an array for identifying gene expression (mRNA level) in human tissues).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marina Miller whose telephone number is (571)272-6101. The examiner can normally be reached on M-F 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D. can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marina Miller
Examiner
Art Unit 1631

MARJORIE MORAN
PATENT EXAMINER

MM

Marjorie A. Moran
2/10/05